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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/230,048	03/12/99	FLECKENSTEIN	B	058315/0129

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EXAMINER	
KERR, J	
ART UNIT	PAPER NUMBER
1633	14

DATE MAILED: 06/20/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/230,048	FLECKENSTEIN ET AL.	
	Examiner	Art Unit	
	Janet Kerr	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-20 and 28-35* is/are pending in the application.

4a) Of the above claim(s) *13-15,17,29-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-12,16,18-20,28,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

Response to Amendment

The amendment filed 4/3/01, and the supplemental amendment, filed 4/10/01, have been entered.

Applicant's marked up version of the claim amendments is not reflective of the clean copy of the amended claims. To expedite prosecution, the examiner will examine the clean copy of the claims. However, applicant should submit a marked up version of the amended claims which is consistent with the clean copy as per 37 CFR 1.121. Please see the attached Changes to the Patent Rules notice for the proper way of amending claims.

Claim 7 has been canceled.

Claims 1-6, 8-20, and 28-35 remain pending.

Claims 13-15, 17, 29-33 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 6.

Claims 1-6, 8-12, 16, 18-20, 28, 34, and 35 are being examined on the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

The disclosure remains objected to because of the following informalities: the section entitled "Legends" on page 7 of the instant application should be changed to "Brief Description of the Drawings" and should be inserted after the Brief Summary of the Invention and prior to the Detailed Description of the Invention.

The disclosure also remains objected to for the reasons set forth in the Office action of 10/3/00, Paper No. 9. Although it is asserted on pages 5 and 6 of applicant's Response that the specification has been amended to overcome the informalities cited in the last Office action, only a

request for including section designations (as per pages 1-2 of the amendment filed 4/3/01, Paper No. 11) has been submitted.

Appropriate correction is required. Please see the attached Changes to the Patent Rules notice for the proper way of amending the specification.

Claim Rejections - 35 USC § 112

Claims 8-12, 16, 19, 34, and 35 are/remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons of record and the reasons below.

The new matter rejection of claims 18 and 19 has been withdrawn as a pharmaceutical composition is within the scope of a medicament disclosed in the instant application. Applicants have argued that claims 18, 19, 34, and 35 have been amended to recite "A composition which may be used..." (see page 7 of applicants' Response). However, no such amendment to the claims has been submitted.

Amended claims 9-11 (and claims dependent thereon) recite the limitation "consisting essentially of". However, there is no support in the specification or claims as originally filed of nucleic acid molecules "consisting essentially of", nor does the specification define the phrase "consisting essentially of". Applicants are required to cancel the claims or amend the claims such that the claimed invention is supported by the disclosure in the instant application. It is noted that applicants have not indicated where support for the newly recited limitations can be found in the specification. This is a new matter rejection.

Claims 34 and 35 are directed to a method of culturing cells comprising adding to a cell culture a cell growth-stimulating amount of v-IL-6 (claim 34) wherein the cells are selected from B-lymphocytes, hybridomas, hemopoietic or endothelial cells (claim 35). As stated in the previous Office action, the phrase "a cell growth-stimulating amount of v-IL-6", added by

amendment, is new matter as the phrase is neither supported by the teachings in the specification nor the claims as originally filed. The specification, on page 6, part v) discloses a process of growing cells in a culture medium comprising v-IL-6, or v-IL-6 mutants, variants, fragments, or mixtures thereof. There is no support in the specification of "a cell growth-stimulating amount of v-IL-6". Moreover there is no support in the specification or claims as originally filed for the new limitation "which may be used in treatment". It is suggested that applicants amend claim 34 by removing the phrases to overcome this rejection.

Claim 8 is directed to a fragment of v-IL-6 which competitively inhibits the biological activity of IL-6 in a suitable assay system. However, the specification does not provide any amino acid sequences of such fragments which inhibit the biological activity of IL-6, what biological activity of IL-6 is inhibiting, or which assay is suitable for detecting competitive inhibition. The limited information provided in the specification is not deemed sufficient to reasonably convey to one skilled in the art that applicants were in possession of fragments of v-IL-6 which are capable of competitively inhibiting the biological activity of IL-6 in a suitable assay system, at the time the application was filed.

Applicant's arguments filed 4/3/01 have been fully considered but they are not persuasive. It is argued that the knowledge of how to determine which fragments work and which fragments bind to the receptor and competitively inhibit native binding of IL-6 in vivo previously was known. Applicant refers to the discussion on page 2 of Appendix C (see pages 9-10 of applicants' Response). It is unclear to which discussion applicants are referring. Three references were provided in Appendix C, a reference by Burger *et al.* (Blood, 1998), a reference by Wang *et al.* (J. Virology, 2001), and a Tutorial on Searching Sequence Databases by Nicholas *et al.* The only reference which has a page 2 is the Tutorial and this is directed to database searching, not to IL-6/IL-6-receptor interactions. It is requested that applicants clarify the argument.

Claim 12 is directed to an isolated nucleic acid molecule which hybridizes under stringent conditions to the nucleotide sequence of Figure 2. However, the specification fails to disclose

nucleic acid molecules other than those provided by SEQ ID NOS. As discussed in the previous Office action, there are numerous variables which impact on the capability of a polynucleotide to hybridize to any other polynucleotide hybridization of nucleic acid molecules is a function of numerous variables include size and base composition of the nucleic acid molecules, length of homologous base sequences, hybridization conditions including incubation time and temperature, etc. (see, e.g., pages 8 and 9 of the previous Office action). As different hybridization conditions will impact on the nucleic acid molecules which will hybridize to the probe, i.e., SEQ ID NO: 2, and in view of the lack of written description in the specification as to particular hybridization conditions, the skilled artisan could not ascertain, *a priori*, the structures of the nucleic acid molecules encompassed by the claim.

Applicant's arguments filed 4/3/01 have been fully considered but they are not persuasive. It is argued that the concept of stringency is inherently present in the specification and discussed in one or more of the cited publications. It is further argued that Figure 1 provides data relating to stringency and shows the consensus obtained among human, mouse, and HHV IL-6 and further shows positions of greater and less great homology. It is asserted that stringency of hybridization is one aspect of this comparison, with greater stringency being associated with greater homology shown in Figure 1 and lower stringency being associated with lesser homology (see page 10 of applicants' Response). These arguments are not persuasive as a figure showing the amino acid alignment and the consensus sequence of three homologues of IL-6 is not predictive of the ability of the nucleic acid molecules encoding these sequences to hybridize to each other or any other "homologous" nucleic acid sequence. It is further argued that the term "stringent" is well known in the art (see page 11 of applicants' Response). This is not persuasive. Stringency is a relative term. The specification does not disclose hybridization or wash temperatures or salt concentrations of the hybridization solutions, two parameters which are well known in the art to alter the degree of hybridization of nucleic acid molecules.

In the Supplemental Response, filed 4/10/01, it is argued that the teachings described by Carrico was not routine hybridization conditions but a simplified technique that unskilled workers

could follow to obtain hybridization. It is asserted that the specification does not require further explanation of what is already known, and that determining stringency conditions has become very routine and easy to do (see pages 2 and 3 of applicants' Response filed 4/10/01). These arguments are not persuasive. Carrico was relied upon to teach that numerous variables impact on the nucleic acid molecules which will hybridize to a probe. One of skill in the art could not envisage the structural features (i.e., nucleic acid sequences), nor could one of skill in the art reproducibly obtain the claimed nucleic acid molecules as the specification does not disclose the hybridization conditions in which to obtain the claimed nucleic acid molecules. Thus, while the specification discloses the prior art mouse and human IL-6 sequences, and discloses the HHV IL-6 nucleic acid sequence, the specification does not provide the structure of any other sequences which hybridize to the nucleic acid sequence of v-IL-6. The rejection is maintained.

Claims 8, 12, 18, 19, 34, and 35 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons of record and the reasons below.

Claims 8, 12, 18, 19, 34, and 35 are not enabled as the specification does not provide sufficient guidance for one of skill in the art to make and use the v-IL-6 fragment of claim 8, the hybridizable nucleic acid sequence of claim 12, the pharmaceutical compositions of claims 18 and 19, the cell culture media of claim 20, the method of culturing cells of 34, and 35, or the polypeptide fragment of claim 28 for the reasons set forth on pages 10-13 in the Office action of 10/3/00.

Applicants argument with respect to claims 8 and 12 are not persuasive for the reasons set forth above in the Written Description rejection.

With respect to the pharmaceutical compositions of claims 18 and 19, it is argued that applicants have amended the claims by deleting the term "pharmaceutical" (see page 7 of

applicants' Response). This argument is not persuasive as the term "pharmaceutical" has not been deleted from the claims. In addition, the claims remain rejected for the reasons set forth on pages 11 and 12 of the previous Office action. It is noted that applicants have not addressed this aspect of the rejection.

With regard to claims 34 and 35, it is argued that the specification teaches that the desired property of using v-IL-6 arises from the homology to human IL-6, and further that it is known in the art what "suitable cell culture media and suitable cell culture conditions" entail. This is not persuasive as the specification only teaches a process of growing cells in culture comprising culturing the cells in medium comprising v-IL-6. There is no objective evidence in the specification that addition of v-IL-6 stimulates cell growth, or which cells would necessarily respond to v-IL-6 such that cell growth occurs. Moreover, the claims are not enabled as newly amended claim 34 recites the limitation "which may be used in treatment". There is no disclosure of what type of treatment is encompassed, what types of cells are to be used in the treatment, or how any treatment protocols using the cultured cells.

Claims 1, 2, 4-6, 8-12, 16, 18-20, 28, 34, and 35 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 9, 10, and 28 remain vague and indefinite by the phrase "obtained by recombinant expression of the DNA of human herpes virus type 8 (HHV-8)" because HHV-8 DNA encodes a number of proteins, thus it is unclear how the viral interleukin-6 obtained by the method can be "isolated", i.e., it is unclear if the v-IL-6 is isolated from other proteins expressed by HHV-8 or is it isolated from a host cell which expresses HHV-8 DNA.

Claims 4 and 5 remain vague and indefinite by the use of upper and lower case lettering when reciting the amino acid sequence for the reasons of record.

Claim 9 is rendered vague and indefinite by the phrase "isolated nucleic acid molecule coding consisting essentially of the sequence of SEQ ID NO: 1" as there is no definition of "consisting essentially of" in the specification; it is unclear what other sequences can be included or are excluded from the nucleic acid molecule. The metes and bounds of the claim are unclear. In addition, it is unclear what is meant by coding consisting essentially of, is the the term "coding" in the phrase is a typographical error? It is suggested that applicants amend claim 9 to "An isolated nucleic acid molecule consisting of the sequence of SEQ ID NO:1 which encodes v-IL-6".

Claims 10 and 11 are rendered vague and indefinite by the phrase "isolated nucleic acid molecule coding consisting essentially of the sequence of SEQ ID NO: 2" as there is no definition of "consisting essentially of" in the specification; it is unclear what other sequences can be included or are excluded from the nucleic acid molecule. The metes and bounds of the claim are unclear. In addition, SEQ ID NO: 2, as set forth on page 7 of the specification, is indicated as an amino acid sequence, not a nucleic acid sequence. It is unclear what applicants are claiming.

Claim 12 remains vague and indefinite for the reasons of record, i.e., it is unclear what conditions are encompassed as "stringent" as there is no definition either in the claim or in the specification as to which hybridization conditions are deemed "stringent conditions"; and it is unclear if the phrase "encoding functional v-IL-6" is describing the nucleic acid of claim 11 or the isolated nucleic acid molecule which hybridizes to the nucleic acid of claim 11.

Claim 16 is rendered vague and indefinite because only one component of the test kit is recited, i.e., the nucleic acid molecule of claim 11. It is unclear how the nucleic acid molecule, in and of itself, can detect v-IL-6 DNA or RNA. There appears to be missing components in the test kit. The claim is also vague and indefinite by the phrase "isolated nucleic acid molecule coding consisting essentially of the sequence of SEQ ID NO: 1" as there is no definition of "consisting essentially of" in the specification; it is unclear what other sequences can be included or are excluded from the nucleic acid molecule. The metes and bounds of the claim are unclear.

Claim 18 remains vague and indefinite by the phrase "polypeptide as claimed in claim 2" as it is unclear which polypeptide is being claimed (see the rejection of claim 2, above).

Claim 34 is rendered vague and indefinite by the phrase "a cell growth-stimulating amount of v-IL-6" as neither the claim nor the specification disclose any amount of v-IL-6 which stimulates cell growth of any cell type. See also the new matter rejection above.

Claim 35 remains vague and indefinite by the term "hemopoetic" for the reasons of record.

Applicant's arguments filed 4/3/01 have been fully considered but they are not persuasive. It is argued that the use of upper and lower case lettering designates homology among amino acid sequences which is well recognized in the art (see page 14 of applicants' Response). This is not persuasive as designation of homologous amino acid residues is not relevant to the claimed invention. The claim is directed to a polypeptide fragment, per se, and it is suggested that applicants amend the claim such that the fragment is designated in either upper case or lower case lettering.

Claim Rejections - 35 USC § 102

Claims 9-12 and 16 remain rejected under 35 U.S.C. 102(b) as being anticipated by Zhong *et al.*, or Chang *et al.*, for the reasons of record and the reasons below.

The claims are directed to an isolated nucleic acid molecule consisting essentially of the sequence of SEQ ID NO: 1. Note that although claims 10 and 11 recite SEQ ID NO: 2, SEQ ID NO: 2 is an amino acid sequence, not a nucleic acid sequence. These claims are being interpreted as being directed to the nucleic acid sequence, not the amino acid sequence.

Both Zhong *et al.* and Chang *et al.* teach HHV-8 polynucleotides which inherently comprise the nucleic acid sequence encoding v-IL-6 of the instant application.

Applicant's arguments filed 4/3/01 have been fully considered but they are not persuasive.

It is argued that neither of the references teach a nucleic acid molecule consisting essentially of SEQ ID NO: 1 (see page 15 of applicants' Response). This argument is not

persuasive. As set forth in the above 35 U.S.C. 112 first and second paragraph rejections, the specification does not define what nucleotides are included or excluded by the phrase "consisting essentially of". As such, the claimed nucleic acid sequences are not limited to those of SEQ ID NO: 1 and thus encompass the HHV-8 polynucleotides of Zhong *et al.* and Chang *et al.*

Applicants should amend the phrase "consisting essentially of" to "consisting of" to overcome the 35 U.S.C. 102(b) rejections.

No claims are allowed.

This application contains claims 13-15, 17, and 29-33 drawn to an invention nonelected with traverse in Paper No. 8. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet M. Kerr whose telephone number is (703) 305-4055. Should the examiner be unavailable, inquiries should be directed to Deborah Clark, Supervisory Primary Examiner of Art Unit 1633, at (703) 305-4051. Any administrative or procedural questions should be directed to Kimberly Davis, Patent Analyst, at (703) 305-3015. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-7401.

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